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What is new within staging of care for people with dementia? –

The IDEAL schedule and other recent work

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Abstract

Purpose of review: This review provides an overview of recent progress within work centred around the 'International schedule for the integrated assessment and staging of care for dementia' (IDEAL schedule), and places it within the context of recent work around other staging models for dementia.

Recent findings: The IDEAL schedule assesses the severity of dementia across seven dimensions. A 'Menu of care options' of recommended priorities for interventions accompanies the schedule. A user manual for the schedule has just been published. Other staging models for dementia include those based on biomarkers, such as in the recently published research framework for Alzheimer's disease by the National Institute on Aging and Alzheimer's Association (NIA-AA), or those based on specific aspects of dementia, principally cognitive impairment.

Summary: The IDEAL schedule is a global staging model to guide the organisation of dementia care. The schedule covers a range of domains that extend beyond cognitive functioning and include care needs; it is applicable to all types and stages of dementia; and can be used by any health care professional, both within clinical practice and research. The schedule is not in opposition to, or is even complementary to, other staging models for dementia.

Key words: dementia; staging; assessment; care

Introduction

This review is centred around work that has been ongoing by the International Dementia Alliance (IDEAL) group. Our group, formed in 2002 (formerly European Dementia Consensus Network (EDCON)), consists of European specialists from various disciplines with experience in the research, diagnosis and care of patients with dementia.

The IDEAL group started to develop a global staging model in 2011 because of our concerns around the increasing prevalence and burden of dementia [1, 2], as well as the lack of organisation and coordination of dementia care within Europe [3]. In addition, staging, in which diseases or disorders are assessed according to their different severity levels, had led to an improvement in care for other physical and mental disorders, such as cancer and renal-disease [4-9], bipolar disorder [10-14], schizophrenia [10, 12, 15-17], and depression [10, 16-19]. However, our group had found through a systematic review that there was a lack of clinical staging scales for dementia that were able to monitor disease progress and health care needs, were sufficiently validated, showed adequate reliability, were applicable during the entire course of the disease, and were applicable cross-culturally [20], as well as being able to assess both dementia-related and non-dementia-related care needs.

The IDEAL group named our global staging model the 'International schedule for the integrated assessment and staging of care for dementia' (IDEAL schedule), and our aim was for it to be used to organise the care of people with dementia, and thus guide the organisation of dementia care. The five criteria initially laid out by our group for the IDEAL schedule were: i) ease of use; ii) reliability; iii) 'goodness of fit', i.e. for it to record the relevant facts about the patient's condition; iv) for it to have been tried and found useful in different cultures and services; and v) for it to have a direct link to suggestions concerning treatment. The IDEAL schedule is also applicable to all types and stages of dementia, and can be used either within clinical practice or research.

This narrative review provides an overview of recent progress within this work, and places it within the wider research and clinical context of developments within staging for dementia over the last 18 months. Relevant publications have been included in this review that were known to the author group, as well as those identified through a non-systematic search of the literature.

Recent work on the IDEAL schedule

The IDEAL schedule consists of seven dimensions: activities of daily living; physical health; cognitive functioning; behavioural and psychological symptoms; social support; informal care (which includes two sub-dimensions: time spent on care by informal carer; and carer stress); and formal professional care (which includes three sub-dimensions: total number of hours of formal professional care received; total number of hours of formal professional care needed; and additional dementia-related care needed). Each of the seven dimensions is rated on a six-point scale from 0 to 5, with a higher score reflecting a higher level of abnormality/severity. Each dimension has a set of anchor points, which assist the user of the schedule in rating the different dimensions appropriately, and which are described in more detail in a glossary that accompanies the schedule. A total sum score, which can range between 0 and 35, can also be calculated by adding up the individual scores of the seven dimensions. The IDEAL schedule may thereby give a preliminary indication of the overall level of care required (denoted by the total sum score), as well as provide more detailed information about the symptoms of dementia and requirements for care (denoted by the seven individual dimensions).

The IDEAL schedule is also accompanied by a 'Menu of care options', which entails recommended priorities for interventions (though not all possible interventions) for each of the different symptoms and severity patterns of dementia, as measured by the schedule. The aim of this 'Menu of care options' is to enable practitioners to choose appropriate interventions, depending on the patient's

symptomatology and severity levels, as well as their setting and the resources they have available. The 'Menu of care options' includes five categories of interventions: Individualized psychosocial support, **D**rugs, **E**ducation, **A**dditional health problems, and **L**iving arrangements. Within each of these categories, there are listed examples of potential interventions according to the different severity levels of dementia (as measured by the IDEAL schedule), as well as whether the intensity of care is likely to be low, medium or high for each of the categories.

The IDEAL schedule was originally published in preliminary form as part of a journal article on its development and reliability testing across nine countries (France; Germany; Italy; Netherlands; Romania; Serbia; South Korea; Spain; and Turkey) [21]. During this study, the IDEAL schedule was shown to have good inter-rater reliability when two raters (one interviewer, one silent observer) separately completed the schedule based on an interview with a total of 209 dementia patients and their informal caregivers (intraclass correlation coefficients (ICCs) for total IDEAL sum scores ranged between 0.89 and 0.99 in the nine field-sites, and 84.4% of all ICCs were over 0.7 for the individual dimensions of the schedule). Face validity and content validity of the schedule were established through expert consensus of a wide range of professionals involved in dementia care in Europe about the schedule's format and content (e.g. through focus group discussions) [21]. Following this, a paper was published on the inter-rater reliability of the schedule in Ireland (ICCs ranged between 0.77 and 1.0 for the individual dimensions), as well as its criterion validity whereby the 'cognitive functioning' and 'carer stress' (sub-)dimensions of the IDEAL schedule, as well as its total sum score, were correlated with the Clinical Dementia Rating (CDR) scale ($p=0.82$ for 'cognitive functioning'; $p=0.77$ for total sum score) and Zarit Burden interview respectively ($p=0.56$) as a measure of criterion validity [22]. A further study from the Netherlands reported on the development and validation of a version that is completed by informal caregivers, the IDEAL-IC, by correlating this new version with the original clinician-administered IDEAL schedule ($r=0.7$) and the Clinical Dementia Rating sum of boxes (CDR-SB) ($r=0.65$) as a measure of construct validity [23]. In this latter study, correlation between the original IDEAL schedule and the CDR-SB was also very high ($r=0.85$) [23].

This review is timely in that the IDEAL schedule has just been published as part of a detailed manual, which provides the reader with all information needed when learning to use the schedule [24]. This could be any health care professional with experience in the diagnosis, guidance or treatment of people with dementia. In addition, in the last 18 months, work has been completed on the reliability of the IDEAL schedule in a further seven countries (Brazil; China; Croatia; Hong Kong; India; Singapore; and Switzerland) with a total of 174 dementia patients and their caregivers, which found that the schedule had good inter-rater reliability and was easy to use across these different settings and with a variety of different types of health workers. This was complemented by a survey of 23 professionals from 14 countries who had experience in use of the IDEAL schedule, which demonstrated the feasibility and acceptability of the schedule. A paper on this is forthcoming (by Semrau et al). There have also been publications on the reliability and validity of the schedule both in China [25] and Spain [26], which reported good results in these settings. Both of these studies confirmed the main psychometric properties of the original English version of the IDEAL schedule (China: ICC for total sum score for inter-rater reliability = 0.93; Spain: mean ICC for inter-rater reliability = 0.861, 85% of the ICCs over 0.8) and documented the convergent validity of individual items by correlating the total sum score of the IDEAL schedule with the CDR ($p=0.72$), CDR-SB ($p=0.74$), Mini-Mental State Examination (MMSE) ($p=-0.65$) and Caregiver Burden Inventory (CBI) ($p=0.7$) in China [25], and the CDR in Spain ($r=0.63$, r = between 0.4 and 0.84 for individual dimensions) [26]. In addition, both studies contributed further novel findings in that the one from Spain supported a latent construct consistent with the concept of 'care needs' by means of factor analysis [26], and the one from China reported test-retest reliability of the IDEAL schedule for the first time whereby the IDEAL schedule was completed by the same interviewer and silent rater a second time seven to ten days later with the same patients (interclass coefficient for the total IDEAL sum score was 0.95 for interviewers and 0.93 for silent raters) [25].

A new research framework for Alzheimer's disease

In the last 18 months, one issue that is new and relevant to the staging and definition of dementia, and thereby the IDEAL schedule, is the staging proposed implicitly in the new research framework for Alzheimer's disease by the National Institute on Aging and Alzheimer's Association (NIA-AA) [27]. This model represents a shift in thinking about Alzheimer's disease in that it involves the development of a staging system for the condition based on biological criteria, whereby it is defined within research (not clinical practice) by its underlying aggregate of neuropathologic changes, which can be established either through biomarkers in living persons or alternatively an autopsy post-mortem, rather than the clinical signs and symptoms of the disease. Within this model, staging severity of Alzheimer's disease is done via a combination of the grading of disease severity through use of biomarkers and the grading of severity of cognitive impairments [27]. Apart from the NIA-AA, other authors have also similarly published papers in the last 18 months, linking biomarkers to different stages of Alzheimer's disease [28-30].

The IDEAL staging system is not in opposition to this present development of a staging model for Alzheimer's dementia based on biological criteria. Indeed, the IDEAL schedule and the NIA-AA research framework share some similar goals, for example in terms of aiming to create a common language amongst professionals [24, 27]. However, the IDEAL staging model for dementia takes a different approach to the NIA-AA research framework in that it aims to help organise care for any type of dementia (not just Alzheimer's disease) regardless of the clinical presentation and underlying aetiology, and covers not only the degree of cognitive impairment, but also related behavioural and psychological symptoms and functional impairment, and all relevant domains associated with dementia and care needs. Furthermore, the NIA-AA research framework is restricted to research, whereas the IDEAL schedule was primarily developed for clinical practice (though it is also applicable to research). The two approaches are therefore complementary, and indeed the NIA-AA

acknowledge that their research framework is not meant to restrict other models that do not use biomarkers [27].

There have been some criticisms of the NIA-AA research framework, for example that it is too restrictive in terms of basing the definition of Alzheimer's disease purely on a biomarker profile without the requirement for corresponding symptoms; that the designated biomarkers are not sensitive or specific to the clinical diagnosis of dementia; and that – even though the framework is meant to apply to research only – it has implications far beyond that including within clinical practice [31].

Recent work on other staging tools

An alternative approach that has been used within the staging of dementia is based on severity of cognitive impairment through use of established tools that measure cognition, such as the MMSE [32]. For example, previous work by Santabárbara et al (2016) [33] found an increased risk of dementia associated with the severity level of cognitive impairment, as measured by the MMSE. Within this model, agreed cut-off scores are used to differentiate between dementia severity stages. Recent work in the last 18 months has extended this staging model to other population groups. For instance, Chua et al (2018) [34] validated this approach within a multi-ethnic Asian population in Singapore; they found that the cut-off scores that they derived were lower than the conventional scores, and that scores differed between participants of different education levels, which is consistent with previous research [35]. The authors therefore concluded that MMSE cut-off staging scores need to be established according to the locality and specific population group [34].

Lima et al (2017) [36] evaluated the diagnostic validity of another tool that measures cognitive impairment, the CDR-SB. The authors looked at the instrument's ability to detect and stage cognitive impairment amongst patients in Brazil with low educational attainment, and found the tool to have

good validity for this. The CDR is a well-established and widely used scale to measure the severity of cognitive impairments, ranging from normal functioning to severely impaired [37]. The CDR-SB provides an alternative, simpler way of calculating the global sum score of the CDR [36].

Also in Brazil, Lima-Silva et al (2018) [38] explored and found to be satisfactory the factor structure, internal consistency, reliability and convergent reliability of the Brazilian version of the Frontotemporal Dementia Rating Scale (FTD-FRS), which was originally developed in 2010 and includes six stages of severity, ranging from very mild to advanced/profound for frontotemporal dementia [39]. The FTD-FRS differs from the MMSE and CDR staging methods in that it measures functional deterioration across five domains that extend beyond cognitive functioning, including behaviour, outing and shopping, household chores, self-care and mobility.

These staging approaches are again different but not in opposition to the IDEAL staging model. Whilst the MMSE and CDR staging methods are based purely on cognitive impairments, the IDEAL schedule takes a broader approach in that it covers not only cognitive functioning but a range of domains beyond that, including importantly staging of care needs. The MMSE and CDR can thus in fact be incorporated within IDEAL assessments, by providing information in regards to cognitive impairment; an assessment of cognitive impairment conducted through the MMSE or CDR could therefore map onto the 'Cognitive functioning' dimension of the IDEAL schedule, and the IDEAL manual that has just been published includes guidance to do so for the MMSE [24]. Similarly, the FTD-FRS is more restricted than the IDEAL schedule in that it applies only to people with frontotemporal dementia, and does not cover as many domains, for example care aspects beyond self-care. Indeed, one key aspect of the IDEAL schedule is that it was developed to estimate the need for care, rather than functionality, as does the FTD-FRS and other functioning scales.

Conclusion

The IDEAL schedule was developed in response to gaps within dementia staging, and takes a broad approach in that it covers a range of domains that extends beyond cognitive impairments (as some other dementia staging tools do), it is applicable to all types and stages of dementia, and it can be used by any health care professional, both within clinical practice and research. The schedule's reliability and validity has already been established in a wide range of settings using different language versions, though we invite others' to test the schedule in further contexts. In addition, the schedule is unique in that it is accompanied by recommended priorities for interventions for the different symptoms and severity patterns of dementia – the 'Menu of care options'.

The IDEAL staging model is not in opposition, and may even be complementary, to other staging approaches, such as that based on biomarkers, or other staging tools that grade the severity of specific aspects of dementia, particularly cognitive functioning/impairment. We therefore hope that the IDEAL schedule will be used widely, to facilitate the assessment and staging of care for dementia, and ultimately improve the care for people with dementia.

Key points

- The IDEAL schedule is a global staging model, which aims to guide the organisation of dementia care; covers a range of seven domains that extend beyond cognitive functioning and include care needs; is applicable to all types and stages of dementia; and can be used by any health care professional, both within clinical practice and research.
- Other recent work on staging for dementia includes models based on biomarkers in Alzheimer's disease, such as in the recently published research framework by the National Institute on Aging and Alzheimer's Association (NIA-AA), or those based on specific aspects of dementia, principally cognitive impairment, for example the Mini-Mental State Examination (MMSE) or Clinical Dementia Rating Scale (CDR).
- The IDEAL schedule is different to the staging models above, since it takes a broader approach in that it aims to help organise care for any type and stage of dementia regardless of the clinical presentation and underlying aetiology; and it covers not only the degree of cognitive impairment, but also related behavioural and psychological symptoms and functional impairment, and all relevant domains associated with dementia and care needs.
- However, the IDEAL schedule is not in opposition to, or may even be complementary to, these other staging models for dementia.

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Conflicts of interest

None.

References

- [1] Prince MJ, Bryce R, Albanese E et al. The global prevalence of dementia: A systematic review and meta-analyses. *Alzheimer's & Dementia*. 2013; 9: 63-75
- [2] World Health Organization (WHO). Factsheet N°362 on Dementia – A public health priority. 2012
- [3] Waldemar G, Phung KT, Burns A et al. Access to diagnostic evaluation and treatment for dementia in Europe. *Int J Geriatr Psychiatry*. 2007; 22(1):47-54
- [4] Cao D, Vollmer RT, Luly J et al. Comparison of 2004 and 1973 World Health Organization grading systems and their relationship to pathologic staging for predicting long-term prognosis in patients with urothelial carcinoma. *Urology*. 2010; 76(3):593-599
- [5] Edge SB, Compton CC (2010) The American Joint Committee on Cancer: The 7th edition of the *AJCC Cancer Staging Manual* and the future of TNM. *Annals of Surgical Oncology*. 2010; 17:1471-1474
- [6] Hallan SI, Matsushita K, Sang Y et al. *JAMA*. 2012; 308(22):2349-2360
- [7] Heusch P, Nensa F, Schaarschmidt B et al. Diagnostic accuracy of whole-body PET/MRI and whole-body PET/CT for TNM staging in oncology. *Eur J Nucl Mol Imaging*. 2015; 42(1):42-48
- [8] Li J, Guo BC, Sun LR et al. TNM staging of colorectal cancer should be reconsidered by T stage weighting. *World J Gastroenterol*. 2014; 20(17): 5104-5112
- [9] Wang J, Wu N, Zheng QF et al. Evaluation of the 7th edition of the TNM classification in patients with resected esophageal squamous cell carcinoma. *World J Gastroenterol*. 2014; 20(48):18397-18403.
- [10] Cosci F, Fava GA. Staging of mental disorders: Systematic review. *Psychother Psychosom*. 2013; 82:20-34
- [11] Kapczinski F, Dias VV, Kauer-Sant'Anna M et al. Clinical implications of a staging model for bipolar disorders. *Expert Rev Neurother*. 2009; 9:957-966
- [12] McGorry PD, Hickie IB, Yung AR et al. Clinical staging of psychiatric disorders: a heuristic framework for choosing earlier, safer and more effective interventions. *Aust NZ J Psychiatry*. 2006; 40:616-622
- [13] McNamara RK, Nandagopal JJ, Strakowski SM, DelBello MP. Preventive strategies for early-onset bipolar disorder: towards a clinical staging model. *CNS Drugs*. 2010; 24:983-996
- [14] Vieta E, Reinares M, Rosa AR. Prognosis and staging in bipolar disorder. *Actas Esp Psiquiatr*. 2010; 38(suppl. 3):35-38
- [15] Agius M, Goh C, Ulhaq S, McGorry P. The staging model in schizophrenia, and its clinical implications. *Psychiatr Danub*. 2010; 22:211-220

[16] Fava GA, Kellner R. Staging: a neglected dimension in psychiatric classification. *Acta Psychiatr Scand*. 1993; 87:225-230

[17] Lieberman JA, Perkins D, Belger A et al. The early stages of schizophrenia: speculations on pathogenesis, pathophysiology, and therapeutic approaches. *Biol Psychiatry*. 2001; 50:884-897

[18] Fava GA, Tossani E. Prodromal stage of major depression. *Early Interv Psychiatry*. 2007; 1:9-18

[19] Hetrick SE, Parker AG, Hickie IB et al. Early identification and intervention in depressive disorders: towards a clinical staging model. *Psychother Psychosom*. 2008; 77:263-270

[20] Olde Rikkert MG, Tona KD, Janssen L et al. Validity, reliability, and feasibility of clinical staging scales in dementia: a systematic review. *Am J Alzheimers Dis Other Dement*. 2011; 26(5):357-365

[21] Semrau M, Burns A, Djukic-Dejanovic S et al. Development of an international schedule for the assessment and staging of care for dementia. *Journal of Alzheimer's Disease*. 2015; 44(1):139-151

[22] Schepens ME, Lutomski JE, Bruce I et al. Reliability and validity of the International Alliance Schedule for the Assessment and Staging of Care in Ireland. *Am J Geriatric Psychiatry*. 2016; 24(4):297-300

[23] Richters A, Melis RJF, Olde Rikkert MGM, van der Marck MA. The International Dementia Alliance Instrument for Feasible and Valid Staging of Individuals with Dementia by Informal Caregivers. *Journal of the American Geriatrics Society*. 2016; 64(8):1674-1678

* [24] Semrau M, Burns A, Lobo A et al. *Assessment and staging of care for people with dementia: The IDEAL schedule and its user manual*. 2019; Oxford: Oxford University Press

This manual is the first publication, which contains a full final version of the IDEAL schedule, including its accompanying glossary, and the 'menu of care options' of recommended priorities of interventions for the different symptoms and severity patterns of dementia. The manual contains all of the information needed to learn how to use the IDEAL schedule, including resources for training.

* [25] Wang X, Sun Z, Xiong L et al. Reliability and validity of the international dementia alliance schedule for the assessment and staging of care in China. *BMC Psychiatry*. 2017; 17(1):371

This paper is the first to report on the reliability and validity of the Chinese (Mandarin) version of the IDEAL schedule. Apart from confirming the psychometric properties of the original English version of the schedule, the study documents test-retest reliability of the schedule and the convergent validity of individual items for the first time.

* [26] Lopez-Anton R, Barrada JR, Santabarbara J et al. Reliability and Validity of the Spanish version of the IDEAL Schedule for assessing Care Needs in Dementia: Cross-sectional, Multicenter Study. *International Journal of Geriatric Psychiatry*. 2018; 33(3):482-488

This paper is the first to report on the reliability and validity of the Spanish version of the IDEAL schedule. Apart from confirming the psychometric properties of the original English version of the schedule, the study documents the convergent validity of the schedule's individual items for the first time, and reports on a factor analysis that supports a latent construct consistent with the concept of 'care needs'.

* [27] Jack Jr CR, Bennett DA, Blennow K et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimers Dementia*. 2018; 14(4):535-562

This paper is important to staging of dementia, since it implicitly includes the development of a staging model for Alzheimer's disease as part of the Research Framework for Alzheimer's Disease by The National Institute on Ageing and Alzheimer's Association, which is based on biological criteria such as biomarkers and represents a shift in thinking about the condition.

[28] Gangishetti U, Howell JC, Perrin RJ et al. Non-beta-amyloid/tau cerebrospinal fluid markers inform staging and progression in Alzheimer's disease. *Alzheimer's Research and Therapy*. 2018; 10:98

[29] Lorenzi M, Filippone M, Frisoni GB et al. Probabilistic disease progression modeling to characterize diagnostic uncertainty: Application to staging and prediction in Alzheimer's disease. *NeuroImage*. 2017; doi: 10.1016/j.neuroimage.2017.08.059

[30] Williams SM, Schulz P, Rosenberry TL et al. Blood-based oligomeric and other protein variant biomarkers to facilitate pre-symptomatic diagnosis and staging of Alzheimer's disease. *Journal of Alzheimer's Disease*. 2017; 58: 23-35

* [31] McCleery J, Flicker L, Richard E, Quinn TJ. When is Alzheimer's not dementia—Cochrane commentary on The National Institute on Ageing and Alzheimer's Association Research Framework for Alzheimer's Disease. *Age and Ageing*. 2018; doi: 10.1093/ageing/afy167

This paper is important because it provides a critical analysis of the Research Framework for Alzheimer's Disease by The National Institute on Ageing and Alzheimer's Association. The critiques relate to the model divorcing neuropathology from the clinical syndrome; the emphasis placed on one dementia subtype; validity of available biomarkers; the changing meaning of the term 'Alzheimer's disease'; and the potential for a research framework to influence clinical practice.

[32] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*. 1975; 12: 189-198

[33] Santabàrbara J, Lopez-Anton R, Gracia-García P et al. Staging cognitive impairment and incidence of dementia. *Epi and Psych Sciences*. 2016; 25(6):562-572

- [34] Chua XY, Choo RWM, Ha NHL et al. Mapping modified Mini-Mental State Examination (MMSE) scores to dementia stages in a multi-ethnic Asian population. *Int Psychogeriatrics*. 2018; doi:10.1017/S1041610218000704
- [35] Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the Mini-Mental State Examination by age and educational level. *JAMA*. 1993; 269(18): 2386-91
- [36] Lima APV, Castilhos R, Chaves MLF. The use of the Clinical Dementia Rating Scale Sum of Boxes Scores in detecting and staging cognitive impairment/dementia in Brazilian patients with low educational attainment. *Alzheimer Dis Assoc Disord*. 2017; 31: 322-327
- [37] Hughes CP, Berg L, Danziger WL et al. A new clinical scale for the staging of dementia. *British Journal of Psychiatry*. 1982; 140:566-572
- [38] Lima-Silva TB, Bahia VS, Cecchini MA et al. Validity and reliability of the Frontotemporal Dementia Rating Scale (FTD-FRS) for the progression and staging of dementia in Brazilian patients. *Alzheimer Dis Assoc Disord*. 2018; 32: 220-225
- [39] Mioshi E, Hsieh S, Savage S et al. Clinical staging and disease progression in frontotemporal dementia. *Neurology*. 2010; 74:1591-1597